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NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
NEWS 24 Sep 16 Experimental properties added to the REGISTRY file
NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985

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=> s (cre or lox or flp or frt) and recombinase
L1 3018 (CRE OR LOX OR FLP OR FRT) AND RECOMBINASE

=> s (self or auto)(s)(inactivat? or excisi?)
L2 2647 (SELF OR AUTO)(S)(INACTIVAT? OR EXCISI?)

=> s l1 and l2
L3 24 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 15 DUP REM L3 (9 DUPLICATES REMOVED)

=> d ti so l-15

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2002 ACS
TI Self-excising polynucleotides containing the .phi.C31 recombinase gene for use in dicot and monocot plants
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2002 ACS
TI Tissue-specific self-inactivating gene therapy vector containing Loxp sequence and Cre recombinase gene
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2

L4 ANSWER 3 OF 15 MEDLINE DUPLICATE I
TI Identification of genes differentially regulated by glucocorticoids and progestins using a Cre/loxP-mediated retroviral promoter-trapping strategy.
SO JOURNAL OF MOLECULAR ENDOCRINOLOGY, (2002 Jun 28 (3) 177-92.
Journal code: 8902617. ISSN: 0952-5041.

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2002 ACS
TI Self-extinguishing recombinases and their use in expression vectors and genetic engineering
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2002 ACS
TI A system to control the expression of a given gene using another gene that encodes a polypeptide with recombinant activity
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2

L4 ANSWER 6 OF 15 MEDLINE DUPLICATE 2
TI **Cre recombinase-mediated inactivation of H-2D^d transgene expression: evidence for partial missing self-recognition by Ly49A NK cells.**
SO JOURNAL OF IMMUNOLOGY, (2001 Dec 1) 167 (11) 6256-62.
Journal code: 2985117R. ISSN: 0022-1767.

L4 ANSWER 7 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Development of lentiviral vectors encoding **Cre recombinase** for conditional genetic modification in the mouse.
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 2345.
print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.

L4 ANSWER 8 OF 15 MEDLINE DUPLICATE 3
TI **Self-excising retroviral vectors encoding the Cre recombinase overcome Cre-mediated cellular toxicity.**
SO MOLECULAR CELL, (2001 Jul) 8 (1) 233-43.
Journal code: 9802571. ISSN: 1097-2765.

L4 ANSWER 9 OF 15 MEDLINE DUPLICATE 4
TI **FLP-mediated recombination for use in hybrid plant production.**
SO PLANT JOURNAL, (2000 Aug) 23 (3) 423-30.
Journal code: 9207397. ISSN: 0960-7412.

L4 ANSWER 10 OF 15 MEDLINE
TI Stable transduction of actively dividing cells via a novel adenoviral/episomal vector.
SO MOLECULAR THERAPY, (2000 Apr) 1 (4) 314-22.
Journal code: 100890581. ISSN: 1525-0016.

L4 ANSWER 11 OF 15 MEDLINE DUPLICATE 5
TI Targeting genes for **self-excision** in the germ line.
SO GENES AND DEVELOPMENT, (1999 Jun 15) 13 (12) 1524-8.
Journal code: 8711660. ISSN: 0890-9369.

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS
TI Retrovirus gene therapy that **self-inactivate** by sequence-specific recombination
SO Ger. Offen., 10 pp.
CODEN: GWXXBX

L4 ANSWER 13 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Self-deleting retrovirus vectors for gene therapy.
SO Journal of Virology, (1996) Vol. 70, No. 8, pp. 4927-4932.
ISSN: 0022-538X.

L4 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2002 ACS
TI Excision of specific DNA-sequences from integrated retroviral vectors via site-specific recombination
SO Nucleic Acids Research (1995). 23(21), 4551-6
CODEN: NARHAD; ISSN: 0305-1048

L4 ANSWER 15 OF 15 MEDLINE DUPLICATE 6
TI **FLP recombinase** in transgenic plants: constitutive activity in stably transformed tobacco and generation of marked cell clones in *Arabidopsis*.
SO PLANT JOURNAL, (1995 Nov) 8 (5) 637-52.
Journal code: 9207397. ISSN: 0960-7412.

=> d ibib ab 12,11,9,8,5,4,2,1

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:207663 CAPLUS

DOCUMENT NUMBER: 126:196108
TITLE: **Retrovirus gene therapy that self-inactivate** by sequence-specific recombination
INVENTOR(S): von Melchner, Harald; Grez, Manuel; Russ, Andreas
Peter
PATENT ASSIGNEE(S): von Melchner, Harald, Germany; Grez, Manuel; Russ,

Andreas Peter
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19530412	A1	19970220	DE 1995-19530412	19950818
WO 9707223	A1	19970227	WO 1996-EP761	19960223
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,				
ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,				
LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,				
SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AZ, BY, KG, KZ,				
MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,				
IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR				
AU 9649410	A1	19970312	AU 1996-49410	19960223
EP 845041	A1	19980603	EP 1996-905788	19960223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 11511018	T2	19990928	JP 1996-508854	19960223
PRIORITY APPLN. INFO.: DE 1995-19530412 A 19950818				
WO 1996-EP761 W 19960223				

AB Retroviral gene therapy vectors that eliminate sequences not assocd. with

the therapeutic expression cassette after integration into the target cell are described. The elimination of non-essential sequences from the target cell helps to avoid drawbacks assocd. with the use of retroviral vectors, such as the activation of protooncogenes. The elimination of these sequences is brought about by incorporating a site-specific **recombinase** system into the vector. The construction of a Moloney murine leukemia virus expression vector with a **Cre recombinase** gene under control of the pgk promoter incorporated into the U3 region of the 5'-LTR is described. The viral genome also included a pair of loxP elements. Successful deletion of the sequence between the loxP sites was demonstrated in transfected NIH3T3 cells.

L4 ANSWER 11 OF 15 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999315626 MEDLINE
DOCUMENT NUMBER: 99315626 PubMed ID: 10385621
TITLE: **Targeting genes for self-excision in the germ line.**
AUTHOR: Bunting M; Bernstein K E; Greer J M; Capecchi M R; Thomas K R
CORPORATE SOURCE: Hematology Division, Department of Internal Medicine, University of Utah, Salt Lake City, Utah 84112, USA.
SOURCE: GENES AND DEVELOPMENT, (1999 Jun 15) 13 (12) 1524-8.
Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF169416
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990805

AB A procedure is described that directs the self-induced deletion of DNA sequences as they pass through the male germ line of mice. The testes-specific promoter from the angiotensin-converting enzyme gene was used to drive expression of the **Cre-recombinase** gene. **Cre** was linked to the selectable marker Neor, and the two genes flanked with loxP elements. This cassette was targeted to the Hoxa3 gene in mouse ES cells that were in turn used to generate chimeric mice. In these chimeras, somatic cells derived from the ES cells retained the cassette, but **self-excision** occurred in all ES-cell-derived sperm.

L4 ANSWER 9 OF 15 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000481127 MEDLINE
DOCUMENT NUMBER: 20387037 PubMed ID: 10929135
TITLE: **FLP**-mediated recombination for use in hybrid plant production.

AUTHOR: Luo H; Lyznik L A; Gidoni D; Hodges T K
CORPORATE SOURCE: Department of Botany and Plant Pathology, Purdue

University, West Lafayette, IN 47907, USA.
SOURCE: PLANT JOURNAL, (2000 Aug) 23 (3) 423-30.
Journal code: 9207397. ISSN: 0960-7412.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001010

AB We have studied the feasibility in *Arabidopsis* of using a site-specific recombination system **FLP/FRT**, from the 2 microm plasmid of yeast, for making plant hybrids. Initially, *Arabidopsis* plants expressing the **FLP** site-specific **recombinase** were crossed with plants transformed with a vector containing kanamycin-resistance gene (npt) flanked by **FRT** sites, which also served to separate the CaMV35S promoter from a promoterless *gusA*. Hybrid progeny were tested for **excision** of the npt gene and the positioning of 35S promoter proximal to *gusA*. GUS activity was observed in the progeny of all crosses, but not in the progeny derived from the self-pollinated homozygous parents. We then induced male sterility in *Arabidopsis* plants using the antisense expression of a pollen- and tapetum-specific gene, *bcp1*, flanked by **FRT** sites. Upon cross-pollination of flowers on the same male-sterile plants with pollen from **FLP**-containing plants, viable seeds were produced and the progeny hybrid plants developed normally. Molecular analyses revealed that the antisense expression cassette of *bcp1* had been excised in these plants. These results show for the first time that a site-specific **recombinase** can be used to restore fertility in male-sterile plants, providing an alternative method for the production of hybrid seeds and plants.

L4 ANSWER 8 OF 15 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001465205 MEDLINE
DOCUMENT NUMBER: 21403274 PubMed ID: 11511376
TITLE: **Self-excising** retroviral vectors encoding the **Cre recombinase** overcome **Cre**-mediated cellular toxicity.

AUTHOR: Silver D P; Livingston D M
CORPORATE SOURCE: The Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA 02115, USA.
CONTRACT NUMBER: K08CA82572 (NCI)
SOURCE: MOLECULAR CELL, (2001 Jul) 8 (1) 233-43.
Journal code: 9802571. ISSN: 1097-2765.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010821
Last Updated on STN: 20010917
Entered Medline: 20010913

AB The **Cre-lox** system is often used to manipulate sequences in mammalian genomes. We have observed that continuous

expression of the **Cre recombinase** in cultured cells lacking exogenous **lox** sites caused decreased growth, cytopathic effects, and chromosomal aberrations. **Cre** mutants defective in DNA cleavage were not geno- or cytotoxic. A **self-excising** retroviral vector that incorporates a negative feedback loop to limit the duration and intensity of **Cre** expression avoided measurable toxicity, retained the ability to excise a target sequence flanked by **lox** sites, and may provide the basis of a less toxic strategy for the use of **Cre** or similar **recombinases**.

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:676973 CAPLUS
DOCUMENT NUMBER: 135:237592
TITLE: A system to control the expression of a given gene using another gene that encodes a polypeptide with recombinant activity
INVENTOR(S): Herrera, Pedro L.; Fuhrmann-Benzakein, Edya; Vassalli, Jean-Dominique; Metzger, Daniel; Chambon, Pierre
PATENT ASSIGNEE(S): Universite de Geneve, Switz.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066774	A1	20010913	WO 2001-IB336	20010308
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1134287	20010919	EP 2000-810196	20000308	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.: EP 2000-810196	A	20000308		
AB The invention, in the field of medicine and mol. biol., concerns a system to control the expression of a gene of interest, either in vitro or in vivo. It involves a first DNA sequence comprising a gene of interest				

linked in functional relation to a promoter, and a second DNA sequence comprising a second gene that encodes a polypeptide having a recombinant activity specific for target DNA sequences, and two of said target DNA sequences flanking one of the said two DNA sequences. According to the invention, the said second DNA sequence is located between the said promoter and said gene of interest. Another object of the invention is

a DNA vector for the transfection of cells characterized in that it contains at least the system of the invention. The invention also concerns a self excision DNA cassette constituted by a DNA sequence flanked by target DNA sequences comprising at least a gene that encodes an inducible polypeptide having a recombinant activity specific for said target DNA sequences. This self-excision DNA cassette may be used as a blocking sequence that prevent the expression of a given gene under the control of a promoter.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:781104 CAPLUS

DOCUMENT NUMBER: 135:340187

TITLE: Self-extinguishing recombinases and their use in expression vectors and genetic engineering

INVENTOR(S): Livingston, David M.; Silver, Daniel P.

PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, USA

SOURCE: PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001079471	A2	20011025	WO 2001-US12193	
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20010412

WO 2001079471 A3 20020328

W: CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE, TR

US 2002062489 A1 20020523 US 2001-834778 20010412

PRIORITY APPLN. INFO.: US 2000-196338P P 20000412

AB Nucleic acid mols. are provided comprising at least a first signal site and a recombinase gene operably linked to an expression control sequence. Upon entry into a cell, there is a first signal site and a second signal site positioned to mediate excision of a sufficient portion

of either the recombinase gene or the expression control sequence to extinguish recombinase activity when the first and second signal sites are contacted with a recombinase. Self-excision by a selected recombinase (Cre or Flp) of its own coding sequence limits the duration and intensity of the recombinase expression so that the recombinase expression is sufficient for deletion of a sequence flanked on each side by a signal site, and then further recombinase expression is terminated. In one example, two signal sequences (e.g., loxP sites) in a second nucleic acid mol. are in the same, or direct, orientation with respect to one another. Such signal sequences can flank the target gene so that expression of the recombinase results in excision of the target gene and inactivation of expression of the target gene; flank a pos. regulatory element of the target gene so that expression of the recombinase results in excision of the pos. regulatory element and inactivation of

expression of the target gene; or flank a neg. regulatory element of the

target gene so that expression of the recombinase results in excision of the neg. regulatory element and activation of expression of

the target gene. This system eliminates recombinase-mediated toxicity or other undesired effects, but yet retains the ability to effect site-specific recombination. Vectors of the invention are useful as research reagents, as well in the in vivo controlled delivery of diagnostic and therapeutic agents, and in the prodn. of agriculturally important transgenic plants, transgenic animals useful in research, and transgenic proteins.

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:72255 CAPLUS

DOCUMENT NUMBER: 136:113803

TITLE: Tissue-specific self-inactivating gene therapy vector containing LoxP sequence and Cre recombinase gene

INVENTOR(S): Curiel, David T.; Reynolds, Paul N.

PATENT ASSIGNEE(S): Uab Research Foundation, USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002006451	A1	20020124	WO 2001-US22407	
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20010717

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002022018 A1 20020221 US 2001-907186 20010717

PRIORITY APPLN. INFO.: US 2000-219242P P 20000718

AB The present invention provides a strategy that allows for selective switching off of both transgene and viral gene expression in tissues where

such expression is undesirable. The present invention employs a vector

contg. a tissue specific promoter that drives expression of Cre recombinase gene in tissue where transgene expression is undesirable. As a result of Cre recombinase expression, the same or another vector that expresses the transgene in that tissue will be cut by the actions of the Cre recombinase into several pieces due to LoxP sites that are strategically placed within the vector backbone. Consequently, unwanted

transgene as well as viral gene expression are prevented.

REFERENCE COUNT: 3 THERE ARE 3 CITED

REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:157997 CAPLUS

DOCUMENT NUMBER: 136:211873

TITLE: **Self-excising polynucleotides containing the .phi.C31 recombinase gene for use in dicot and monocot plants**

INVENTOR(S): Mankin, Luke

PATENT ASSIGNEE(S): Basf Plant Science G.m.b.H., Germany; McKersie, Bryan

SOURCE: PCT Int. Appl. 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2002016609 A2 20020228 WO 2001-US26738
20010827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ,
CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT,
BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG
AU 2001088439 A5 20020304 AU 2001-88439 20010827
PRIORITY APPLN. INFO.: US 2000-227961 P P 20000825
WO 2001-US26738 W 20010827

AB The present invention includes compns. and methods for providing organisms

from which transgenic traits can be easily excised. More specifically, the present invention provides **self-excising** polynucleotides that contain a desired trait and a **recombinase** polynucleotide operably linked to a promoter, all flanked by a pair of directly oriented recombination sites, wherein the **recombinase** activity is regulatable. More preferably, the .phi.C31 **recombinase** contg. an intron such that the **recombinase** is not expressed in bacteria such as Agrobacteria, but the **recombinase** is expressed in eukaryotes such as plants. Expression in bacteria is also limited through the use of a promoter that is active in eukaryotes such as plants, but inactive in bacteria such as Agrobacteria. Thus, a binary vector (pBPS EW051) is constructed that

contains the .phi.C31intINT **recombinase** gene controlled by the TOP10 promoter, a tetracycline-repressed transactivator gene controlled by

the octopine synthase promoter. The **self-excising** cassette from vector pBPS EW051 is validated in planta using Arabidopsis

thaliana as a representative dicotyledonous plant. **Self-excising** T-DNA vectors for monocotyledonous plants also contain the **recombinase** gene .phi.C31intINT with or without an intron, in a tetracycline-repressed gene regulation system comprising a binary

vector similar to that used for dicots, except that the selectable marker

is the modified AHAS gene for resistance to the imidazolinone herbicides.

The **self-excising** .phi.C31int cassette is validated for monocotyledonous plants in planta using perennial ryegrass (Lolium perenne) as a typical monocotyledonous plant. The present invention provides methods for the elimination of unwanted nucleic acids in agricultural food products. Addnl., the compns. and methods of the

present invention provide a means to prevent the escape of certain transgenic traits into the environment.

=> d his

(FILE 'HOME' ENTERED AT 15:11:54 ON 15 OCT 2002)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 15:12:07 ON
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L1 3018 S (CRE OR LOX OR FLP OR FRT) AND
RECOMBINASE
L2 2647 S (SELF OR AUTO)(S)(INACTIVAT? OR EXCISI?)
L3 24 S L1 AND L2
L4 15 DUP REM L3 (9 DUPLICATES REMOVED)

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	47.58	47.79

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
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	-3.10	-3.10

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STN INTERNATIONAL SESSION SUSPENDED AT 15:26:05 ON 15
OCT 2002

Connecting via Winsock to STN

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LOGINID:SSSPATA1636DXS

PASSWORD:

***** RECONNECTED TO STN INTERNATIONAL *****
SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS' AT
16:02:46 ON 15 OCT 2002
FILE 'MEDLINE' ENTERED AT 16:02:46 ON 15 OCT 2002
FILE 'BIOSIS' ENTERED AT 16:02:46 ON 15 OCT 2002
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FILE 'CAPLUS' ENTERED AT 16:02:46 ON 15 OCT 2002
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
SINCE FILE TOTAL

CA SUBSCRIBER PRICE	ENTRY	SESSION
	-3.10	-3.10

=> dhis

DHIS IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d his

(FILE 'HOME' ENTERED AT 15:11:54 ON 15 OCT 2002)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 15:12:07 ON
15 OCT 2002
L1 3018 S (CRE OR LOX OR FLP OR FRT) AND
RECOMBINASE
L2 2647 S (SELF OR AUTO)(S)(INACTIVAT? OR EXCISI?)
L3 24 S L1 AND L2
L4 15 DUP REM L3 (9 DUPLICATES REMOVED)

=> s selfexcis? or autoexcis?

L5 12 SELFEXCIS? OR AUTOEXCIS?

=> s l1 and l5

L6 0 L1 AND L5

=> s toxic?

L7 1409345 TOXIC?

=> s l1(s)l7

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'L1(S)L22'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'L2(S)L23'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'L3(S)L24'

L8 81 L1(S) L7

=> dup rem l8

PROCESSING COMPLETED FOR L8

L9 50 DUP REM L8 (31 DUPLICATES REMOVED)

=> d ti so 30-50

L9 ANSWER 30 OF 50 MEDLINE

DUPLICATE 12

TI Ectopic expression of the bHLH gene Math1 disturbs neural development.

SO EUROPEAN JOURNAL OF NEUROSCIENCE, (1999 Jul) 11 (7) 2582-8.

Journal code: 8918110. ISSN: 0953-816X.

L9 ANSWER 31 OF 50 MEDLINE

DUPLICATE 13

TI Selectable marker-free transgenic plants without sexual crossing: transient expression of **cre recombinase** and use of a conditional lethal dominant gene.

SO PLANT MOLECULAR BIOLOGY, (1999 May) 40 (2) 223-35.

Journal code: 9106343. ISSN: 0167-4412.

L9 ANSWER 32 OF 50 MEDLINE

DUPLICATE 14

TI An adenoviral vector deleted for all viral coding sequences results in enhanced safety and extended expression of a leptin transgene.

SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF

AMERICA, (1998 Jul 7) 95 (14) 7866-71.

Journal code: 7505876. ISSN: 0027-8424.

L9 ANSWER 33 OF 50 MEDLINE

DUPLICATE 15

TI Inducible expression based on regulated recombination: a single vector strategy for stable expression in cultured cells.

SO NUCLEIC ACIDS RESEARCH, (1998 Jul 1) 26 (13) 3263-9.

Journal code: 0411011. ISSN: 0305-1048.

L9 ANSWER 34 OF 50 MEDLINE

DUPLICATE 16

TI Efficient Fas-ligand gene expression in rodent liver after intravenous injection of a recombinant adenovirus by the use of a **Cre**-mediated switching system.

SO GENE THERAPY, (1998 Aug) 5 (8) 1047-53.

Journal code: 9421525. ISSN: 0969-7128.

L9 ANSWER 35 OF 50 MEDLINE

TI Two transgenic approaches to define the cell lineages in endocrine pancreas development.

SO MOLECULAR AND CELLULAR ENDOCRINOLOGY, (1998 May 25) 140 (1-2) 45-50.

Journal code: 7500844. ISSN: 0303-7207.

L9 ANSWER 36 OF 50 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI A transgenic mouse line that retains **Cre recombinase** activity in mature oocytes irrespective of the **cre** transgene transmission.

SO Biochemical and Biophysical Research Communications, (1997)

Vol. 237, No.

2, pp. 318-324.

ISSN: 0006-291X.

L9 ANSWER 37 OF 50 MEDLINE

TI How knockout mouse lines will be used to study the role of drug-metabolizing enzymes and their receptors during reproduction and development, and in environmental **toxicity**, cancer, and oxidative stress.

SO BIOCHEMICAL PHARMACOLOGY, (1997 Feb 7) 53 (3) 249-

54. Ref: 44

Journal code: 0101032. ISSN: 0006-2952.

L9 ANSWER 38 OF 50 CAPLUS COPYRIGHT 2002 ACS

TI Recombinational cloning using engineered recombination sites

SO PCT Int. Appl., 106 pp.

CODEN: PIXXD2

L9 ANSWER 39 OF 50 MEDLINE

DUPLICATE 17

TI Production and characterization of human 293 cell lines expressing the

site-specific **recombinase Cre**.

SO SOMATIC CELL AND MOLECULAR GENETICS, (1996 Nov 22) (6) 477-88.

Journal code: 8403568. ISSN: 0740-7750.

L9 ANSWER 40 OF 50 MEDLINE

TI A new transgenic mouse mutagenesis test system using Spi- and 6-thioguanine selections.

SO ENVIRONMENTAL AND MOLECULAR MUTAGENESIS, (1996) 28 (4) 465-70.

Journal code: 8800109. ISSN: 0893-6692.

L9 ANSWER 41 OF 50 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

18

TI Inducible ternary control of transgene expression and cell ablation in Drosophila.

SO Development Genes and Evolution, (1996) Vol. 206, No. 1, pp. 14-24.

ISSN: 0949-944X.

L9 ANSWER 42 OF 50 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI **Cre**-mediated site-specific translocation between nonhomologous mouse chromosomes.

SO Proceedings of the National Academy of Sciences of the United States of

America, (1995) Vol. 92, No. 16, pp. 7376-7380.

ISSN: 0027-8424.

L9 ANSWER 43 OF 50 MEDLINE

TI Site-specific integration of DNA into wild-type and mutant **lox** sites placed in the plant genome.

SO PLANT JOURNAL, (1995 Apr) 7 (4) 649-59.

Journal code: 9207397. ISSN: 0960-7412.

L9 ANSWER 44 OF 50 MEDLINE

TI **FLP recombinase** in transgenic plants: constitutive activity in stably transformed tobacco and generation of marked cell clones in *Arabidopsis*.

SO PLANT JOURNAL, (1995 Nov) 8 (5) 637-52.

Journal code: 9207397. ISSN: 0960-7412.

L9 ANSWER 45 OF 50 MEDLINE

TI Intra-chromosomal rearrangements generated by **Cre-lox** site-specific recombination.

SO NUCLEIC ACIDS RESEARCH, (1995 Feb 11) 23 (3) 485-90.

Journal code: 0411011. ISSN: 0305-1048.

L9 ANSWER 46 OF 50 MEDLINE

TI **Cre recombinase**-mediated site-specific recombination between plant chromosomes.

SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Mar 1) 91 (5) 1706-10.
Journal code: 7505876. ISSN: 0027-8424.

L9 ANSWER 47 OF 50 MEDLINE

TI Functional expression of the yeast **FLP/FRT** site-specific recombination system in *Nicotiana tabacum*.
SO MOLECULAR AND GENERAL GENETICS, (1994 Mar) 242 (6) 653-7.
Journal code: 0125036. ISSN: 0026-8925.

L9 ANSWER 48 OF 50 MEDLINE

TI Exchange of gene activity in transgenic plants catalyzed by the **Cre-lox** site-specific recombination system.
SO PLANT MOLECULAR BIOLOGY, (1992 Jan) 18 (2) 353-61.
Journal code: 9106343. ISSN: 0167-4412.

L9 ANSWER 49 OF 50 MEDLINE

TI Gene transfer with subsequent removal of the selection gene from the host genome.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1991 Dec 1) 88 (23) 10558-62.
Journal code: 7505876. ISSN: 0027-8424.

L9 ANSWER 50 OF 50 MEDLINE

TI Site-directed recombination in the genome of transgenic tobacco.
SO MOLECULAR AND GENERAL GENETICS, (1990 Sep) 223 (3) 369-78.
Journal code: 0125036. ISSN: 0026-8925.

=> d ti so 10-29

L9 ANSWER 10 OF 50 CAPLUS COPYRIGHT 2002 ACS
TI Adenovirus-based methods, and cells, useful for the expression of nucleic acid sequences
SO U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S. Ser. No. 473,168.
CODEN: USXXCO

L9 ANSWER 11 OF 50 MEDLINE DUPLICATE 6
TI Delivery of the **Cre recombinase** by a self-deleting lentiviral vector: efficient gene targeting in vivo.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 Sep 25) 98 (20) 11450-5.
Journal code: 7505876. ISSN: 0027-8424.

L9 ANSWER 12 OF 50 MEDLINE DUPLICATE 7
TI Growth inhibition and DNA damage induced by **Cre recombinase** in mammalian cells.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 Jul 31) 98 (16) 9209-14.
Journal code: 7505876. ISSN: 0027-8424.

L9 ANSWER 13 OF 50 MEDLINE DUPLICATE 8
TI A novel system for mitigation of ectopic transgene expression induced by adenoviral vectors.
SO GENE THERAPY, (2001 Aug) 8 (16) 1271-5.
Journal code: 9421525. ISSN: 0969-7128.

L9 ANSWER 14 OF 50 MEDLINE DUPLICATE 9
TI Development of a **FLP/ft** system for generating helper-dependent adenoviral vectors.
SO MOLECULAR THERAPY, (2001 May) 3 (5 Pt 1) 809-15.
Journal code: 100890581. ISSN: 1525-0016.

L9 ANSWER 15 OF 50 MEDLINE DUPLICATE 10

TI Reduction of **Cre recombinase** toxicity in proliferating *Drosophila* cells by estrogen-dependent activity regulation.

SO DEVELOPMENT GENES AND EVOLUTION, (2001 Sep) 211 (8-9) 458-65.
Journal code: 9613264. ISSN: 0949-944X.

L9 ANSWER 16 OF 50 MEDLINE DUPLICATE 11

TI Self-excising retroviral vectors encoding the **Cre recombinase** overcome **Cre**-mediated cellular toxicity.
SO MOLECULAR CELL, (2001 Jul) 8 (1) 233-43.
Journal code: 9802571. ISSN: 1097-2765.

L9 ANSWER 17 OF 50 MEDLINE

TI Multiple pathways for **Cre/lox**-mediated recombination in plastids.
SO PLANT JOURNAL, (2001 Jul) 27 (2) 161-70.
Journal code: 9207397. ISSN: 0960-7412.

L9 ANSWER 18 OF 50 CAPLUS COPYRIGHT 2002 ACS

TI Delivery of functional protein sequences by translocating polypeptides
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2

L9 ANSWER 19 OF 50 CAPLUS COPYRIGHT 2002 ACS

TI Cells expressing **recombinase Cre** regulated by **recombinase FLP** for use in preparation of recombinant adenovirus vectors
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2

L9 ANSWER 20 OF 50 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI Inactivation of *Pasteurella (Mannheimia) haemolytica* leukotoxin causes partial attenuation of virulence in a calf challenge model.
SO Infection and Immunity, (July, 2000) Vol. 68, No. 7, pp. 3916-3922. print.
ISSN: 0019-9567.

L9 ANSWER 21 OF 50 MEDLINE

TI A radiation-controlled molecular switch for use in gene therapy of cancer.
SO GENE THERAPY, (2000 Jul) 7 (13) 1121-5.
Journal code: 9421525. ISSN: 0969-7128.

L9 ANSWER 22 OF 50 MEDLINE

TI **Cre-lox** site-specific recombination between *Arabidopsis* and tobacco chromosomes.
SO PLANT JOURNAL, (2000 Sep) 23 (6) 715-22.
Journal code: 9207397. ISSN: 0960-7412.

L9 ANSWER 23 OF 50 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI Hepatocyte-specific deletion of the gp130 gene: Consequences for the regulation of the acute-phase response and liver development.
SO Hepatology, (October, 2000) Vol. 32, No. 4 Pt. 2, pp. 197A. print.
Meeting Info.: 51st Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases Dallas, Texas, USA
October 27-31, 2000 American Association for the Study of Liver Diseases
ISSN: 0270-9139.

L9 ANSWER 24 OF 50 MEDLINE

TI "Gene-swap knock-in" cassette in mice to study allelic differences in human genes.
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (2000) 919 148-70.
Journal code: 7506858. ISSN: 0077-8923.

L9 ANSWER 25 OF 50 MEDLINE

TI A new approach for the identification and cloning of genes: the pBACwich system using **Cre/lox** site-specific recombination.
SO NUCLEIC ACIDS RESEARCH, (2000 Apr 1) 28 (7) E19.
Journal code: 0411011, ISSN: 1362-4962.

L9 ANSWER 26 OF 50 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI Caspases are critically involved in hypoxia- and ischemia-induced oligodendrocyte damage.
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract
No.-88.11. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience ISSN: 0190-5295.

L9 ANSWER 27 OF 50 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI A second generation **Cre-lox** system based on trans-synaptic transfer of **Cre recombinase**.
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract
No.-510.9. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience ISSN: 0190-5295.

L9 ANSWER 28 OF 50 CAPLUS COPYRIGHT 2002 ACS

TI Antitumor gene therapy using expression vectors containing the **Cre** /**loxP** recombination system
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2

L9 ANSWER 29 OF 50 CAPLUS COPYRIGHT 2002 ACS

TI Recombinational cloning using engineered recombination sites
SO U.S., 72 pp., Cont.-in-part of U.S. Ser. No. 486,139, abandoned.
CODEN: USXXAM

=> d ibib ab 49,33,31,19

L9 ANSWER 49 OF 50 MEDLINE

ACCESSION NUMBER: 92073325 MEDLINE
DOCUMENT NUMBER: 92073325 PubMed ID: 1660141
TITLE: Gene transfer with subsequent removal of the selection gene

from the host genome.

AUTHOR: Dale E C; Ow D W
CORPORATE SOURCE: Plant Gene Expression Center, U.S. Department of Agriculture/Agricultural Research Service, Albany, CA 94710.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1991 Dec 1) 88 (23) 10558-62.
Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199201
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19920109

AB A general method of gene transfer that does not leave behind a selectable marker in the host genome is described. A luciferase gene was introduced

into the tobacco genome by using the hygromycin phosphotransferase gene

(hpt) as a linked selectable marker. Flanked by recombination sites from

the bacteriophage P1 **Cre/lox** recombination system, the hpt gene was subsequently excised from the plant genome by the **Cre recombinase**. The **Cre**-catalyzed excision event in the plant genome was precise and conservative—i.e., without loss or alteration of nucleotides in the recombinant site. After removal of the **Cre**-encoding locus by genetic segregation, plants were obtained that had incorporated only the desired transgene. Gene transfer without

the incorporation of antibiotic-resistance markers in the host genome should ease public concerns over the field release of transgenic organisms

expressing such traits. Moreover, it would obviate the need for different selectable markers in subsequent rounds of gene transfer into the same host.

L9 ANSWER 33 OF 50 MEDLINE DUPLICATE 15

ACCESSION NUMBER: 1998292548 MEDLINE
DOCUMENT NUMBER: 98292548 PubMed ID: 9628928
TITLE: Inducible expression based on regulated recombination: a

single vector strategy for stable expression in cultured cells.

AUTHOR: Angrand P O; Woodroffe C P; Buchholz F; Stewart A F

CORPORATE SOURCE: Gene Expression Program, EMBL, Meyerhofstrasse 1, D-69117 Heidelberg, Germany.

SOURCE: NUCLEIC ACIDS RESEARCH, (1998 Jul 1) 26 (13) 3263-9.
Journal code: 0411011. ISSN: 0305-1048.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199808

ENTRY DATE: Entered STN: 19980817

Last Updated on STN: 19980817

Entered Medline: 19980805

AB When fused to the ligand binding domain (LBD) of steroid hormone nuclear

receptors, site-specific **recombinases** (SSRs) acquire a ligand-dependent activity. Here, we describe the use of SSR-LBD fusion

proteins in an inducible expression system, introduced into cells in a single step. A single transgene contains a constitutively active, bi-directional enhancer/promoter, which directs expression, on one side,

of an SSR-LBD fusion protein gene and, on the other, a selectable marker/inducible gene cassette. The selectable marker, the puromycin acetyltransferase (pac) gene, is used for stable genomic integration of the transgene and is flanked by recombination target sites. The inducible

gene is not expressed because the pac gene lies between it and the promoter. Activation of the SSR-LBD by a ligand induces recombination and

the pac gene is excised. The inducible gene is thus positioned next to the

promoter and so is expressed. This describes a ligand-inducible expression

strategy that relies on regulated recombination rather than regulated transcription. By inducible expression of diphtheria toxin, evidence that

this system permits inducible expression of very toxic proteins is presented. The combination of the complete regulatory circuit and inducible gene in one transgene relates expression of the selectable marker gene to expression from the bi-directional enhancer/promoter. We

exploit this relationship to show that graded increases in selection

pressure can be used to select for clones with different induction properties.

L9 ANSWER 31 OF 50 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 1999339247 MEDLINE
DOCUMENT NUMBER: 99339247 PubMed ID: 10412902

TITLE: Selectable marker-free transgenic plants without sexual crossing: transient expression of **cre recombinase** and use of a conditional lethal dominant gene.

AUTHOR: Gleave A P; Mitra D S; Mudge S R; Morris B A
CORPORATE SOURCE: Plant Development Group, HortResearch, Auckland, New Zealand.

SOURCE: PLANT MOLECULAR BIOLOGY, (1999 May) 40 (2) 223-35.

Journal code: 9106343. ISSN: 0167-4412.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199908

ENTRY DATE: Entered STN: 19990816

Last Updated on STN: 19990816

Entered Medline: 19990803

AB Transgenic tobacco plants were produced that contained single-copy pART54

T-DNA, with a 35S-uidA gene linked to loxP-flanked kanamycin resistance

(nptII) and cytosine deaminase (codA) genes. Retransformation of these

plants with pCre1 (containing 35S transcribed **cre recombinase** and hygromycin (hpt) resistance genes) resulted in excision of the loxP-flanked genes from the genome. Phenotypes of progeny

from selfed-retransformed plants confirmed nptII and codA excision and

integration of the **cre**-linked hpt gene. To avoid integration of the hpt gene, and thereby generate plants totally free of marker genes, we

attempted to transiently express the **cre recombinase**.

Agrobacterium tumefaciens (pCre1) was cocultivated with leaf discs of two

pART54-transformed lines and shoots were regenerated in the absence of

hygromycin selection. Nineteen of 773 (0.25%) shoots showed tolerance to

5-fluorocytosine (5-fc) which is converted to the **toxic**

5-fluorouracil by cytosine deaminase. 5-fc tolerance in six shoots was found to be due to excision of the loxP-flanked region of the pART54 T-DNA. In four of these shoots excision could be attributed to **cre** expression from integrated pCre1 T-DNA, whereas in two shoots excision

appeared to be a consequence of transient **cre** expression from pCre1 T-DNA molecules which had been transferred to the plant cells but

not integrated into the genome. The absence of selectable marker genes was

confirmed by the phenotype of the T1 progeny. Therefore, through transient

cre expression, marker-free transgenic plants were produced without sexual crossing. This approach could be applicable to the elimination of marker genes from transgenic crops which must be vegetatively propagated to maintain their elite genotype.

L9 ANSWER 19 OF 50 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:260503 CAPLUS

DOCUMENT NUMBER: 132:290501

TITLE: Cells expressing **recombinase Cre** regulated by **recombinase FLP** for use in preparation of recombinant adenovirus vectors

INVENTOR(S): Saito, Izumu; Kanegae, Yumi

PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2000022106 A1 20000420 WO 1999-JP5548 19991007
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH,
CN, CR, CU,
CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL,
IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
MD, MG,
MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL,
TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY,
KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE,
CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1122310 A1 20010808 EP 1999-970420 19991007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT,
IE, SI, LT, LV, FI, RO
AU 9960056 A1 20000501 AU 1999-60056 19991010

PRIORITY APPLN. INFO.: JP 1998-289785 A 19981012
WO 1999-JP5548 W 19991007

AB Cells expressing **recombinase Cre**, which expression is dependent on the presence of **recombinase FLP**, are provided and used for the prepn. of recombinant viral vectors such as adenovirus vectors. The cells are prepnd. by transformation with an expression cassette contg. a strong promoter, a **recombinase FLP**-recognizing sequence, and the gene encoding **recombinase Cre**. The method avoids the cellular toxicity of **Cre**. Prepn. of **FLP**-dependent **Cre**-expressing 293FNCre cells and use of the cells for the prepn. of recombinant adenovirus were demonstrated.

REFERENCE COUNT: 12 THERE ARE 12 CITED

REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d is

'IS' IS NOT A VALID FORMAT

In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.

REENTER DISPLAY FORMAT FOR ALL FILES
(FILEDEFAULT):end

=> d his

(FILE 'HOME' ENTERED AT 15:11:54 ON 15 OCT 2002)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 15:12:07 ON 15 OCT 2002

L1 3018 S (CRE OR LOX OR FLP OR FRT) AND RECOMBINASE

L2 2647 S (SELF OR AUTO)(S)(INACTIVAT? OR EXCISI?)

L3 24 S L1 AND L2

L4 15 DUP REM L3 (9 DUPLICATES REMOVED)

L5 12 S SELFEXCIS? OR AUTOEXCIS?

L6 0 S L1 AND L5

L7 1409345 S TOXIC?

L8 81 S L1(S)L7

L9 50 DUP REM L8 (31 DUPLICATES REMOVED)

=> s transient
L10 405716 TRANSIENT

=> s transient?(2a)express?
L11 31417 TRANSIENT?(2A) EXPRESS?

=> s recombinase
L12 6962 RECOMBINASE

=> s l11(s)l12
L13 77 L11(S) L12

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14 33 DUP REM L13 (44 DUPLICATES REMOVED)

=> s l14 not py>2000
L15 29 L14 NOT PY>2000

=> d ti so 1-29

L15 ANSWER 1 OF 29 MEDLINE
TI N-terminal RAG1 frameshift mutations in Omenn's syndrome: internal
methionine usage leads to partial V(D)J recombination activity and reveals
a fundamental role in vivo for the N-terminal domains.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2000 Dec 19) 97 (26) 14572-7.
Journal code: 7505876. ISSN: 0027-8424.

L15 ANSWER 2 OF 29 MEDLINE
TI Detection and analysis of gene expression during infection by in vivo
expression technology.
SO PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY OF LONDON. SERIES B: BIOLOGICAL SCIENCES, (2000 May 29) 355 (1397) 587-99. Ref: 53
Journal code: 7503623. ISSN: 0962-8436.

L15 ANSWER 3 OF 29 MEDLINE
TI Rapid generation of nested chromosomal deletions on mouse chromosome 2.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2000 Sep 12) 97 (19) 10471-6.
Journal code: 7505876. ISSN: 0027-8424.

L15 ANSWER 4 OF 29 MEDLINE
TI A novel reporter mouse strain that expresses enhanced green fluorescent protein upon Cre-mediated recombination.
SO FEBS LETTERS, (2000 Mar 31) 470 (3) 263-8.
Journal code: 0155157. ISSN: 0014-5793.

L15 ANSWER 5 OF 29 MEDLINE
TI New approach to cell lineage analysis in mammals using the Cre-loxP system.
SO MOLECULAR REPRODUCTION AND DEVELOPMENT, (2000 May) 56 (1) 34-44.
Journal code: 8903333. ISSN: 1040-452X.

L15 ANSWER 6 OF 29 MEDLINE
TI A recombinase-based selection of differentially expressed bacterial genes.
SO GENE, (1999 Nov 15) 240 (1) 99-106.
Journal code: 7706761. ISSN: 0378-1119.

L15 ANSWER 7 OF 29 MEDLINE
TI A mouse model of arterial gene transfer: antigen-specific immunity

is a
minor determinant of the early loss of adenovirus-mediated transgene expression.
SO CIRCULATION RESEARCH, (1999 Oct 29) 85 (9) e25-32.
Journal code: 0047103. ISSN: 1524-4571.

L15 ANSWER 8 OF 29 MEDLINE
TI Reversible immortalization of human myogenic cells by site-specific excision of a retrovirally transferred oncogene.
SO HUMAN GENE THERAPY, (1999 Jul 1) 10 (10) 1607-17.
Journal code: 9008950. ISSN: 1043-0342.

L15 ANSWER 9 OF 29 MEDLINE
TI Selectable marker-free transgenic plants without sexual crossing: transient expression of cre recombinase and use of a conditional lethal dominant gene.
SO PLANT MOLECULAR BIOLOGY, (1999 May) 40 (2) 223-35.
Journal code: 9106343. ISSN: 0167-4412.

L15 ANSWER 10 OF 29 MEDLINE
TI The prokaryotic beta-recombinase catalyzes site-specific recombination in mammalian cells.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Mar 5) 274 (10) 6634-40.
Journal code: 2985121R. ISSN: 0021-9258.

L15 ANSWER 11 OF 29 MEDLINE
TI Using Flp-recombinase to characterize expansion of Wnt1-expressing neural progenitors in the mouse.
SO DEVELOPMENTAL BIOLOGY, (1998 Sep 1) 201 (1) 57-65.
Journal code: 0372762. ISSN: 0012-1606.

L15 ANSWER 12 OF 29 MEDLINE
TI Sustained somatic gene inactivation by viral transfer of Cre recombinase.
SO NATURE BIOTECHNOLOGY, (1996 Nov) 14 (11) 1562-5.
Journal code: 9604648. ISSN: 1087-0156.

L15 ANSWER 13 OF 29 MEDLINE
TI Selective disruption of genes transiently induced in differentiating mouse embryonic stem cells by using gene trap mutagenesis and site-specific recombination.
SO MOLECULAR AND CELLULAR BIOLOGY, (1998 May) 18 (5) 3081-8.
Journal code: 8109087. ISSN: 0270-7306.

L15 ANSWER 14 OF 29 MEDLINE
TI A genetic system that reports transient activation of genes in Bacillus.
SO GENE, (1997 Nov 20) 202 (1-2) 121-6.
Journal code: 7706761. ISSN: 0378-1119.

L15 ANSWER 15 OF 29 MEDLINE
TI Microinjection of cre recombinase RNA induces site-specific recombination of a transgene in mouse oocytes.
SO NUCLEIC ACIDS RESEARCH, (1998 Jan 15) 26 (2) 676-8.
Journal code: 0411011. ISSN: 0305-1048.

L15 ANSWER 16 OF 29 MEDLINE
TI Transient expression of SV 40 large T antigen by Cre/LoxP-mediated site-specific deletion in primary human tumor cells.
SO HUMAN GENE THERAPY, (1997 Sep 20) 8 (14) 1695-700.
Journal code: 9008950. ISSN: 1043-0342.

L15 ANSWER 17 OF 29 MEDLINE
TI Efficient removal of loxP-flanked DNA sequences in a gene-targeted locus

by transient expression of Cre recombinase in fertilized eggs.

SO MOLECULAR REPRODUCTION AND DEVELOPMENT, (1997 Feb) 46 (2) 109-13.
Journal code: 8903333. ISSN: 1040-452X.

L15 ANSWER 18 OF 29 MEDLINE
TI Temporal control of the Cre recombinase in transgenic mice by a tetracycline responsive promoter.
SO NUCLEIC ACIDS RESEARCH, (1996 Oct 1) 24 (19) 3875-7.
Journal code: 0411011. ISSN: 0305-1048.

L15 ANSWER 19 OF 29 MEDLINE
TI FLP-mediated site-specific recombination in microinjected murine zygotes.
SO TRANSGENIC RESEARCH, (1996 Nov) 5 (6) 385-95.
Journal code: 9209120. ISSN: 0962-8819.

L15 ANSWER 20 OF 29 MEDLINE
TI Humanized prion protein knock-in by Cre-induced site-specific recombination in the mouse.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1996 May 24) 222 (3) 742-7.
Journal code: 0372516. ISSN: 0006-291X.

L15 ANSWER 21 OF 29 MEDLINE
TI Regulation of Cre recombinase activity by the synthetic steroid RU 486.
SO NUCLEIC ACIDS RESEARCH, (1996 Apr 15) 24 (8) 1404-11.
Journal code: 0411011. ISSN: 0305-1048.

L15 ANSWER 22 OF 29 MEDLINE
TI High frequency recombination between loxP sites in human chromosomes mediated by an adenovirus vector expressing Cre recombinase.
SO SOMATIC CELL AND MOLECULAR GENETICS, (1995 Nov) 21 (6) 429-41.
Journal code: 8403568. ISSN: 0740-7750.

L15 ANSWER 23 OF 29 MEDLINE
TI A site-directed chromosomal translocation induced in embryonic stem cells by Cre-loxP recombination.
SO NATURE GENETICS, (1995 Apr) 9 (4) 376-85.
Journal code: 9216904. ISSN: 1061-4036.

L15 ANSWER 24 OF 29 MEDLINE
TI Site-specific integration of DNA into wild-type and mutant lox sites placed in the plant genome.
SO PLANT JOURNAL, (1995 Apr) 7 (4) 649-59.
Journal code: 9207397. ISSN: 0960-7412.

L15 ANSWER 25 OF 29 MEDLINE
TI Site-specific recombination of a transgene in fertilized eggs by transient expression of Cre recombinase.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Jan 3) 92 (1) 160-4.
Journal code: 7505876. ISSN: 0027-8424.

L15 ANSWER 26 OF 29 MEDLINE
TI Function and control of recombination-activating gene activity.
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1992 May 4) 651 277-94. Ref: 20
Journal code: 7506858. ISSN: 0077-8923.

L15 ANSWER 27 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Inactivation of the whey acidic protein (WAP) gene by site-specific recombination in mouse embryonic stem cells.
SO Journal of Animal Science and Technology, (December, 2000) Vol. 42, No. 6.

pp. 941-956. print.
ISSN: 0367-5807.

L15 ANSWER 28 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Cre-loxP system confers cell lineage-specific expression of a reporter gene in murine preimplantation development.
SO Journal of Reproduction and Development., (Dec., 1999) Vol. 45, No. 6, pp. 411-417.
ISSN: 0916-8818.

L15 ANSWER 29 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Gene therapy 1998: Transient or stable minigene expression and gene repair/inactivation.
SO Biogenic Amines, (1998) Vol. 14, No. 5, pp. 389-406.
ISSN: 0168-8561.

=> d ibib ab 26,25,22,17,12,9

L15 ANSWER 26 OF 29 MEDLINE
ACCESSION NUMBER: 92286571 MEDLINE
DOCUMENT NUMBER: 92286571 PubMed ID: 1599127
TITLE: Function and control of recombination-activating gene activity.
AUTHOR: Alt F W; Rathbun G; Oltz E; Taccioli G; Shinkai Y
CORPORATE SOURCE: Howard Hughes Medical Institute, Children's Hospital, Boston, Massachusetts.
CONTRACT NUMBER: AI20047 (NIAID)
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1992 May 4) 651 277-94. Ref: 20
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199207
ENTRY DATE: Entered STN: 19920717
Last Updated on STN: 19920717
Entered Medline: 19920709
AB The RAG-1 and RAG-2 genes synergistically confer VDJ recombinase activity to nonlymphoid cell lines. To unequivocally test RAG gene function, we created lines of mice that lack functional copies of these genes. Consistent with the possibility that RAG genes encode the tissue-specific components of VDJ recombinase, RAG-2-deficient mice are viable but have a severe combined immune deficiency due to inability to initiate VDJ recombination and thereby generate mature lymphocytes. RAG-2-deficient mice have no obvious defect in any tissue or lineage other than lymphocytes, indicating that VDJ recombinase activity and RAG-2-gene function is required only for lymphocyte development. Levels of RAG-1 and RAG-2 expression in primary murine lymphoid tissues and lymphoid bone marrow cultures generally are much higher than those of transformed precursor B-cell lines. Low-level RAG gene expression in permanent cell lines results from a decline during propagation due to outgrowth of cells with lower RAG expression levels. The low and variable level of RAG gene expression in transformed pre-B cell lines correlates with low and variable rates of endogenous VDJ recombination; therefore, such lines are not reliable models for

experiments aimed at studying mechanisms that target this activity to particular variable region gene segments. To generate such a system, we

introduced RAG genes into B-lineage lines under the control of a heat

shock-inducible promoter; heat-shock treatment induces extremely high-level but **transient RAG expression** accompanied by parallel induction of **VDJ recombinase** activity. Such cells efficiently rearrange transfected VDJ recombination substrates in a regulated manner that is dependent on the activity of transcriptional control elements associated with the target V gene segments.

L15 ANSWER 25 OF 29 MEDLINE

ACCESSION NUMBER: 95116515 MEDLINE

DOCUMENT NUMBER: 95116515 PubMed ID: 7816809

TITLE: Site-specific recombination of a transgene in fertilized eggs by **transient expression** of Cre recombinase.

AUTHOR: Araki K; Araki M; Miyazaki J; Vassalli P
CORPORATE SOURCE: Department of Pathology, Centre Medical Universitaire,

University of Geneva, Switzerland.

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE

UNITED STATES OF AMERICA, (1995 Jan 3) 92 (1)

160-4.

Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199502

ENTRY DATE: Entered STN: 19950217

Last Updated on STN: 19980206

Entered Medline: 19950209

AB An efficient method of transgene modulation in fertilized eggs has been

developed that uses the Cre/loxP recombination system. Twelve transgenic

mouse lines carrying a chicken beta-actin promoter-loxP-chloramphenicol

acetyltransferase (CAT) gene-loxP-beta-galactosidase gene construct were

produced. After selection of the line showing the highest expression of

the CAT gene in a variety of tissues, eggs of this line were injected in the male or female pronucleus with a Cre expression vector placed under

the control of the chicken beta-actin promoter and kept in a circular form

to avoid genomic integration. This resulted in a transient expression of

Cre in the eggs, leading to recombination of the transgene as detected by

galactosidase expression and DNA analysis. Recombination was completed

before the morula stage with both types of pronuclear injections and occurred with a very high frequency; no mosaicism, no incomplete recombination, and no integration of the Cre sequence were observed in 18

mice born with this modified transgene. The beta-galactosidase gene was

expressed in various tissues at levels comparable to those found for the

CAT gene in the founder line. This Cre transient expression system should

be useful for breeding transgenic lines in which transgene expression leads to sterility or lethality--in particular, for selecting transgenic lines with high expression of a potentially lethal transgene whose full activity is difficult to explore in a conventional transgenic system because of the risk of selecting for transgenic lines carrying only poorly expressed transgenes.

L15 ANSWER 22 OF 29 MEDLINE

ACCESSION NUMBER: 96174442 MEDLINE

DOCUMENT NUMBER: 96174442 PubMed ID: 8600570

TITLE: High frequency recombination between loxP sites in human chromosomes mediated by an adenovirus vector expressing Cre recombinase.

AUTHOR: Wang P; Anton M; Graham F L; Bacchetti S

CORPORATE SOURCE: Department of Pathology, McMaster University, Hamilton, Ontario, Canada.

SOURCE: SOMATIC CELL AND MOLECULAR GENETICS, (1995 Nov) 21 (6) 429-41.

Journal code: 8403568. ISSN: 0740-7750.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199604

ENTRY DATE: Entered STN: 19960513

Last Updated on STN: 19960513

Entered Medline: 19960426

AB An adenovirus vector (AdCre1) expressing Cre recombinase has been used to induce recombination between loxP sites in human chromosomes.

G418 resistant cells with one loxP site, generated by transfection with a

plasmid containing loxP between the SV40 promoter and the G418 resistance

(neo) gene, were infected with AdCre1 and transfected with a plasmid

containing loxP adjacent to a promoterless hisD gene. This resulted in

integration of hisD downstream of the SV40 promoter with gain of histidinol and loss of G418 resistance. Since AdCre1 is non-replicating

and Cre expression transient, histidinol resistant cells containing the hisD gene flanked by loxP sites were stable.

Reinfection of these cells with AdCre1 induced excision of hisD in over

90% of infected cells. This high efficiency of site-specific recombination

suggests that AdCre1 may be exploited for temporal and tissue-specific

regulation of gene expression and for chromosome engineering in vitro and

in animals.

L15 ANSWER 17 OF 29 MEDLINE

ACCESSION NUMBER: 97173843 MEDLINE

DOCUMENT NUMBER: 97173843 PubMed ID: 9021742

TITLE: Efficient removal of loxP-flanked DNA sequences in a gene-targeted locus by **transient expression** of Cre recombinase in fertilized eggs.

AUTHOR: Sunaga S; Maki K; Komagata Y; Ikuta K; Miyazaki J

CORPORATE SOURCE: Department of Disease-Related Gene Regulation Research (Sandoz), Tokyo, Japan.

SOURCE: MOLECULAR REPRODUCTION AND DEVELOPMENT, (1997 Feb) 46 (2) 109-13.

Journal code: 8903333. ISSN: 1040-452X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199704

ENTRY DATE: Entered STN: 19970422

Last Updated on STN: 19970422

Entered Medline: 19970408

AB The bacteriophage P1 Cre/loxP site-specific recombination system is a useful tool for engineering chromosomal changes in animal cells. **Transient expression of the Cre recombinase** gene directly introduced into fertilized eggs by pronuclear injection has been reported to provide an efficient method of transgene modulation in fertilized eggs. In the present study, we examined the efficacy of this method to remove loxP-flanked DNA sequences in a gene-targeted locus in fertilized eggs. We replaced a part of the T-cell receptor gamma (TCR V gamma) locus with homologous sequences containing a loxP-flanked neogene in mouse embryonic stem (ES) cells by gene-targeting technique. The resulting ES cell clones containing the mutant allele (V gamma LNL) were used to generate chimeric mice by blastocyst injection. Eight male chimeras were bred with superovulated wild-type female mice. One hundred and seventy-six fertilized eggs were collected, and subjected to pronuclear injection of the Cre expression plasmid, pCAGGS-Cre, of a covalently closed circular form. Three out of 11 pups inherited the targeted V gamma locus. The inherited targeted allele of these 3 mice was shown to have undergone Cre-mediated recombination, resulting in a deletion of the loxP-flanked sequences (V gamma delta) as shown by Southern blot analysis of DNA from tail biopsies. All 3 founder mutant mice were capable of transmitting the V gamma delta locus to their offspring. The other 8 pups carried only wild-type alleles. There were no pups carrying the unrecombined V gamma LNL locus. Thus, the frequency of Cre-mediated recombination was 100% (3/3) with this method. In contrast, when closed circular pCAGGS-Cre plasmid was introduced into ES cells by electroporation, the recombination frequency of the V gamma LNL locus was 9.6%. These results indicated that our system based on **transient expression of the Cre recombinase** gene directly introduced into fertilized eggs by pronuclear injection provides a fast and efficient method for generating mutant mice with desired deletions or translocations in target genes.

L15 ANSWER 12 OF 29 MEDLINE
ACCESSION NUMBER: 1998298560 MEDLINE
DOCUMENT NUMBER: 98298560 PubMed ID: 9634821
TITLE: Sustained somatic gene inactivation by viral transfer of Cre recombinase.
COMMENT: Comment in: Nat Biotechnol. 1996 Nov;14(11):1537
AUTHOR: Rohlmann A; Gotthardt M; Willnow T E; Hammer R E; Herz J
CORPORATE SOURCE: Department of Molecular Genetics, Howard Hughes Medical Institute, University of Texas Southwestern Medical Center, Dallas 75235, USA.
CONTRACT NUMBER: HL20948 (NHLBI)
SOURCE: NATURE BIOTECHNOLOGY, (1996 Nov) 14 (11) 1562-5.
Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980828
Last Updated on STN: 19980828
Entered Medline: 19980814

AB Transgenic and knockout mice have proven invaluable tools for analyzing physiologically relevant functions of numerous genes. In some cases, however, pleiotropic effects that result from a variable requirement for a particular gene in different tissues, cell types, or stages of embryonic development may complicate the analysis due to a complex phenotype or embryonic lethality. The loxP/Cre-mediated recombination system, which allows tissue-specific gene targeting in the mouse, can be used to overcome these problems. A limitation of current methods is that a carrying a loxP-tagged gene must be crossed with a transgenic mouse expressing the Cre **recombinase** in an appropriate tissue to obtain the desired gene rearrangement. We have used recombinant adenovirus carrying the Cre **recombinase** to induce virtually quantitative somatic cell gene disruption in the liver. The targeted gene was the multifunctional low-density lipoprotein receptor-related protein (LRP), a cell surface receptor for alpha 2-macroglobulin and other ligands. **Transient expression** of Cre following adenoviral infection produced the predicted gene rearrangement, functionally inactivating LRP in the liver. Rearrangement occurred within 6 days after infection and remained stable for at least 28 days. The results demonstrate the suitability of adenoviral Cre gene transfer to induce long-term, quantitative, and temporally controlled gene disruption in the mouse.

L15 ANSWER 9 OF 29 MEDLINE
ACCESSION NUMBER: 1999339247 MEDLINE
DOCUMENT NUMBER: 99339247 PubMed ID: 10412902
TITLE: Selectable marker-free transgenic plants without sexual crossing: **transient expression of cre recombinase** and use of a conditional lethal dominant gene.
AUTHOR: Gleave A P; Mitra D S; Mudge S R; Morris B A
CORPORATE SOURCE: Plant Development Group, HortResearch, Auckland, New Zealand.
SOURCE: PLANT MOLECULAR BIOLOGY, (1999 May) 40 (2) 223-35.
Journal code: 9106343. ISSN: 0167-4412.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990803
AB Transgenic tobacco plants were produced that contained single-copy pART54. T-DNA, with a 35S-uidA gene linked to loxP-flanked kanamycin resistance (nptII) and cytosine deaminase (codA) genes. Retransformation of these plants with pCre1 (containing 35S transcribed cre **recombinase** and hygromycin (hpt) resistance genes) resulted in excision of the loxP-flanked genes from the genome. Phenotypes of progeny from selfed-retransformed plants confirmed nptII and codA excision and integration of the cre-linked hpt gene. To avoid integration of the hpt gene, and thereby generate plants totally free of marker genes, we attempted to **transiently express the cre recombinase**. Agrobacterium tumefaciens (pCre1) was cocultivated with leaf discs of two pART54-transformed lines and shoots were regenerated in the absence of hygromycin selection. Nineteen of 773 (0.25%) shoots showed tolerance to 5-fluorocytosine (5-fc) which is converted to the toxic 5-fluorouracil by cytosine deaminase. 5-fc tolerance in six shoots was found to be due to excision of the loxP-flanked region of the pART54 T-DNA. In four of these shoots

excision

could be attributed to cre expression from integrated pCre1 T-DNA, whereas

in two shoots excision appeared to be a consequence of **transient cre expression** from pCre1 T-DNA molecules which had been transferred to the plant cells but not integrated into the genome. The absence of selectable marker genes was confirmed by the phenotype of the

T1 progeny. Therefore, through **transient cre expression**, marker-free transgenic plants were produced without sexual crossing.

This approach could be applicable to the elimination of marker genes from transgenic crops which must be vegetatively propagated to maintain their elite genotype.

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FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 15:12:07 ON 15 OCT 2002

L1 3018 S (CRE OR LOX OR FLP OR FRT) AND RECOMBINASE

L2 2647 S (SELF OR AUTO)(S)(INACTIVAT? OR EXCISI?)

L3 24 S L1 AND L2

L4 15 DUP REM L3 (9 DUPLICATES REMOVED)

L5 12 S SELFEXCIS? OR AUTOEXCIS?

L6 0 S L1 AND L5

L7 1409345 S TOXIC?

L8 81 S L1(S)L7

L9 50 DUP REM L8 (31 DUPLICATES REMOVED)

L10 405716 S TRANSIENT

L11 31417 S TRANSIENT?(2A)EXPRESS?

L12 6962 S RECOMBINASE

L13 77 S L11(S)L12

L14 33 DUP REM L13 (44 DUPLICATES REMOVED)

L15 29 S L14 NOT PY>2000

=> s (site directed or site specific)(s)recombinase

L16 2027 (SITE DIRECTED OR SITE SPECIFIC)(S) RECOMBINASE

=> s l16 and review

L17 90 L16 AND REVIEW

=> dup rem l17

PROCESSING COMPLETED FOR L17

L18 78 DUP REM L17 (12 DUPLICATES REMOVED)

=> s identify

L19 425920 IDENTIFY

=> s identif?

L20 2125429 IDENTIF?

=> s l18 and l20

L21 8 L18 AND L20

=> d ti so l-8

L21 ANSWER 1 OF 8 MEDLINE

TI Molecular ecology and evolution of *Streptococcus thermophilus* bacteriophages—a review.

SO VIRUS GENES, (1998) 16 (1) 95-109. Ref: 48
Journal code: 8803967. ISSN: 0920-8569.

L21 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI Control of directionality in integrase-mediated recombination: examination of recombination directionality factors (RDFs) including Xis and Cox proteins

SO Nucleic Acids Research (2001), 29(11), 2205-2216

CODEN: NARHAD; ISSN: 0305-1048

L21 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI The transgeneticist's toolbox: novel methods for the targeted modification of eukaryotic genomes

SO Biological Chemistry (2000), 381(9/10), 801-813
CODEN: BICHF3; ISSN: 1431-6730

L21 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI Mobile gene cassettes and integrons: moving antibiotic resistance genes in

Gram-negative bacteria

SO Ciba Foundation Symposium (1997), 207(Antibiotic Resistance: Origins, Evolution, Selection and Spread), 192-205
CODEN: CIBSB4; ISSN: 0300-5208

L21 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI Construction of recombinant cell lines with defined properties using FLP

recombinase driven gene replacement

SO Animal Cell Technology: From Vaccines to Genetic Medicine, [Proceedings of the Meeting of the EACT], 14th, Vilamoura, Port., May 1996 (1997), Meeting Date 1996, 511-517. Editor(s): Carrondo, Manuel J. T.; Griffiths, Bryan; Moreira, Jose L. P. Publisher: Kluwer, Dordrecht, Neth.
CODEN: 64ELAL

L21 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI Mobile gene cassettes and integrons: capture and spread of genes by site-specific recombination

SO Molecular Microbiology (1995), 15(4), 593-600
CODEN: MOMIEE; ISSN: 0950-382X

L21 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI Rearrangement of nif operons in cyanobacterial heterocysts

SO Current Plant Science and Biotechnology in Agriculture (1993), 17(New Horizons in Nitrogen Fixation), 575-80
CODEN: CPBAE2; ISSN: 0924-1949

L21 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI The Fis protein: it's not just for DNA inversion anymore

SO Molecular Microbiology (1992), 6(22), 3257-65
CODEN: MOMIEE; ISSN: 0950-382X

=> d ibib ab 3,2

L21 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:790924 CAPLUS

DOCUMENT NUMBER: 135:832

TITLE: The transgeneticist's toolbox: novel methods for the targeted modification of eukaryotic genomes

AUTHOR(S): Bode, Jürgen; Schlaake, Thomas; Iber, Michaela; Schubeler, Dirk; Seibler, Jost; Snejhov, Evgeny; Nikolaev, Lev

CORPORATE SOURCE: German Center for Biotechnological Research (GBF),

RDIF/Epigenetic Regulation, Braunschweig, D-38124, Germany

SOURCE: Biological Chemistry (2000), 381(9/10), 801-813
CODEN: BICHF3; ISSN: 1431-6730

PUBLISHER: Walter de Gruyter GmbH & Co. KG

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review and discussion with 60 refs. Classical techniques for gene transfer into mammalian cells involve tedious screening procedures to

identify transgenic clones or animals with the appropriate level

and stability of expression or with the correct developmental patterns. These first generation technologies are clearly inadequate for complex genetic strategies by which gene regulation can be studied in its entire complexity. While site-specific insertions can principally be achieved by homologous recombination or by adapting the recombination app. from phages

or yeast, these methods usually lack the required efficiency or they perturb expression patterns by the co-insertion of prokaryotic vector parts. Virtually all of these problems can be overcome by recombinase-mediated cassette exchange (RMCE) techniques which cleanly

replace a resident cassette that is flanked by two hetero-specific recombination target sites for a second cassette with the analogous design, presented on a targeting vector. After illustrating the fundamentals of site-specific recombination by selected expts., the authors (arranged in the chronol. order of their contribution) will describe their efforts to develop RMCE into a method of wide applicability. Further developments that have been initiated utilizing the particular potential of the RMCE principle will be outlined.

REFERENCE COUNT: 60 THERE ARE 60 CITED

REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:440232 CAPLUS

DOCUMENT NUMBER: 136:129808

TITLE: Control of directionality in integrase-mediated recombination: examination of recombination directionality factors (RDFs) including Xis and Cox proteins

AUTHOR(S): Lewis, John A.; Hatfull, Graham F.

CORPORATE SOURCE: Pittsburgh Bacteriophage Institute and Department of

Biological Sciences, University of Pittsburgh, Pittsburgh, PA, 15260, USA

SOURCE: Nucleic Acids Research (2001), 29(11), 2205-2216

CODEN: NARHAD; ISSN: 0305-1048

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB Similarity between the DNA substrates and products of integrase-mediated

site-specific recombination reactions results in a single recombinase enzyme being able to catalyze both the integration and excision reactions. The control of directionality in these reactions is achieved through a class of small accessory factors that favor one reaction while interfering with the other. These proteins,

called recombination directionality factors (RDFs), play architectural roles in reactions catalyzed by their cognate recombinases and have been

identified in conjunction with both tyrosine and serine integrases. Previously identified RDFs are typically small, basic and have diverse amino acid sequences. A subset of RDFs, the cox

genes, also function as transcriptional regulators. The authors present here a compilation of all the known RDF proteins as well as those identified through database mining that the authors predict to be involved in conferring recombination directionality. Anal. of this group

of proteins shows that they can be grouped into distinct sub-groups based

on their sequence similarities and that they are likely to have arisen from several independent evolutionary lineages. This compilation will

prove useful in recognizing new proteins that confer directionality upon

site-specific recombination reactions encoded by plasmids, transposons, phages and prophages.

REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 15:11:54 ON 15 OCT 2002)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 15:12:07 ON 15 OCT 2002

L1 3018 S (CRE OR LOX OR FLP OR FRT) AND RECOMBINASE
L2 2647 S (SELF OR AUTO)(S)(INACTIVAT? OR EXCISI?)
L3 24 S L1 AND L2
L4 15 DUP REM L3 (9 DUPLICATES REMOVED)
L5 12 S SELFEXCIS? OR AUTOEXCIS?
L6 0 S L1 AND L5
L7 1409345 S TOXIC?
L8 81 S L1(S)L7
L9 50 DUP REM L8 (31 DUPLICATES REMOVED)
L10 405716 S TRANSIENT
L11 31417 S TRANSIENT?(2A)EXPRESS?
L12 6962 S RECOMBINASE
L13 77 S L1(S)L12
L14 33 DUP REM L13 (44 DUPLICATES REMOVED)
L15 29 S L14 NOT PY>2000
L16 2027 S (SITE DIRECTED OR SITE SPECIFIC)(S)RECOMBINASE
L17 90 S L16 AND REVIEW
L18 78 DUP REM L17 (12 DUPLICATES REMOVED)
L19 425920 S IDENTIFY
L20 2125429 S IDENTIF?
L21 8 S L18 AND L20

=> D TI SO 1-20

L21 ANSWER 1 OF 8 MEDLINE

TI Molecular ecology and evolution of *Streptococcus thermophilus* bacteriophages--a review.

SO VIRUS GENES, (1998) 16 (1) 95-109. Ref: 48
Journal code: 8803967. ISSN: 0920-8569.

L21 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI Control of directionality in integrase-mediated recombination: examination

of recombination directionality factors (RDFs) including Xis and Cox proteins

SO Nucleic Acids Research (2001), 29(11), 2205-2216
CODEN: NARHAD; ISSN: 0305-1048

L21 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI The transgeneticist's toolbox: novel methods for the targeted modification

of eukaryotic genomes

SO Biological Chemistry (2000), 381(9/10), 801-813
CODEN: BICHF3; ISSN: 1431-6730

L21 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI Mobile gene cassettes and integrons: moving antibiotic resistance genes in

Gram-negative bacteria

SO Ciba Foundation Symposium (1997), 207(Antibiotic Resistance: Origins,

Evolution, Selection and Spread), 192-205
CODEN: CIBSB4; ISSN: 0300-5208

L21 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS

TI Construction of recombinant cell lines with defined properties using FLP

recombinase driven gene replacement

SO Animal Cell Technology: From Vaccines to Genetic Medicine, [Proceedings of

the Meeting of the ESACT], 14th, Vilamoura, Port., May 1996 (1997),
Meeting Date 1996, 511-517. Editor(s): Carrondo, Manuel J. T.;
Griffiths, Bryan; Moreira, Jose L. P. Publisher: Kluwer, Dordrecht, Neth.
CODEN: 64ELAL

L21 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
TI Mobile gene cassettes and integrons: capture and spread of genes by site-specific recombination
SO Molecular Microbiology (1995), 15(4), 593-600
CODEN: MOMIEE; ISSN: 0950-382X

L21 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS
TI Rearrangement of nif operons in cyanobacterial heterocysts
SO Current Plant Science and Biotechnology in Agriculture (1993), 17(New Horizons in Nitrogen Fixation), 575-80
CODEN: CPBAE2; ISSN: 0924-1949

L21 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
TI The Fis protein: it's not just for DNA inversion anymore
SO Molecular Microbiology (1992), 6(22), 3257-65
CODEN: MOMIEE; ISSN: 0950-382X

=> S L18
L22 78 L18

=> S TI SO 1-20
L23 0 TI SO 1-20

=> S L18
L24 78 L18

=> D TI SO 1-20

L24 ANSWER 1 OF 78 MEDLINE
TI When reverse genetics meets physiology: the use of site-specific recombinases in mice.
SO FEBS LETTERS, (2002 Oct 2) 529 (1) 116.
Journal code: 0155157. ISSN: 0014-5793.

L24 ANSWER 2 OF 78 MEDLINE
TI Shufflons: multiple inversion systems and integrons.
SO ANNUAL REVIEW OF GENETICS, (1999) 33 171-91. Ref: 84
Journal code: 0117605. ISSN: 0066-4197.

L24 ANSWER 3 OF 78 MEDLINE
TI Molecular ecology and evolution of *Streptococcus thermophilus* bacteriophages—a review.
SO VIRUS GENES, (1998) 16 (1) 95-109. Ref: 48
Journal code: 8803967. ISSN: 0920-8569.

L24 ANSWER 4 OF 78 MEDLINE
TI Transposition and site-specific recombination: adapting DNA cut-and-paste mechanisms to a variety of genetic rearrangements.
SO FEMS MICROBIOLOGY REVIEWS, (1997 Sep) 21 (2) 157-78.
Ref: 142
Journal code: 8902526. ISSN: 0168-6445.

L24 ANSWER 5 OF 78 MEDLINE
TI Accessibility and the developmental regulation of V(D)J recombination.
SO SEMINARS IN IMMUNOLOGY, (1997 Jun) 9 (3) 161-70. Ref: 65
Journal code: 9009458. ISSN: 1044-5323.

L24 ANSWER 6 OF 78 MEDLINE
TI Site-specific recombination in gram-positive theta-replicating plasmids.
SO FEMS MICROBIOLOGY LETTERS, (1996 Aug 15) 142 (1) 1-10.
Ref: 28

Journal code: 7705721. ISSN: 0378-1097.

L24 ANSWER 7 OF 78 MEDLINE
TI Conjugative transposition.
SO ANNUAL REVIEW OF MICROBIOLOGY, (1995) 49 367-97.
Ref: 108
Journal code: 0372370. ISSN: 0066-4227.

L24 ANSWER 8 OF 78 MEDLINE
TI Phosphoryl transfer in Flp recombination: a template for strand transfer mechanisms.
SO TRENDS IN BIOCHEMICAL SCIENCES, (1994 Feb) 19 (2) 78-82. Ref: 21
Journal code: 7610674. ISSN: 0968-0004.

L24 ANSWER 9 OF 78 MEDLINE
TI Site-specific recombinases: tools for genome engineering.
SO TRENDS IN GENETICS, (1993 Dec) 9 (12) 413-21. Ref: 51
Journal code: 8507085. ISSN: 0168-9525.

L24 ANSWER 10 OF 78 MEDLINE
TI Mechanistic and structural complexity in the site-specific recombination pathways of Int and FLP.
SO CURRENT OPINION IN GENETICS AND DEVELOPMENT, (1993 Oct) 3 (5) 699-707.
Ref: 108
Journal code: 9111375. ISSN: 0959-437X.

L24 ANSWER 11 OF 78 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI Recombinase-directed plant transformation for the post-genomic era.
SO Plant Molecular Biology, (January, 2002) Vol. 48, No. 1-2, pp. 183-200.
<http://www.kluweronline.com/issn/0167-4412>. print.
ISSN: 0167-4412.

L24 ANSWER 12 OF 78 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI "Cre"-ating mouse mutants: A meeting review on conditional mouse genetics (New York, New York, USA; August 31-September 2, 1998; National Cancer Institute.
SO Genes & Development, (Jan. 15, 1999) Vol. 13, No. 2, pp. 142-145.
ISSN: 0890-9369.

L24 ANSWER 13 OF 78 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI ILLEGITIMATE RECOMBINATION IN BACTERIA.
SO BERG, D. E. AND M. M. HOWE (ED.). MOBILE DNA. XVIII+972P. AMERICAN SOCIETY FOR MICROBIOLOGY: WASHINGTON, D.C., USA. ILLUS.
MAPS. (1989) 0 (0), 799-832.
ISBN: 1-55581-005-5.

L24 ANSWER 14 OF 78 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI SITE-SPECIFIC RECOMBINASES CHANGING PARTNERS AND DOING THE TWIST.
SO J. Bacteriol., (1986 (RECD 1987)) 165 (2), 341-347.
CODEN: JOBAAY. ISSN: 0021-9193.

L24 ANSWER 15 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI When reverse genetics meets physiology: the use of site-specific recombinases in mice.
SO FEBS Letters (2002), 529(1), 116-121
CODEN: FEBLAL; ISSN: 0014-5793

L24 ANSWER 16 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Excision of selectable marker genes from transgenic plants

SO Nature Biotechnology (2002), 20(6), 575-580
CODEN: NABIF9; ISSN: 1087-0156

L24 ANSWER 17 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Diversity in the serine recombinases
SO Molecular Microbiology (2002), 44(2), 299-307
CODEN: MOMIEE; ISSN: 0950-382X

L24 ANSWER 18 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Genome engineering using **site-specific recombinases**
SO Cloning and Stem Cells (2002), 4(1), 65-80
CODEN: CSCLBO; ISSN: 1536-2302

L24 ANSWER 19 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Conditional alleles in mice: practical considerations for tissue-specific knockouts
SO Genesis (New York, NY, United States) (2002), 32(2), 49-62
CODEN: GNESFY; ISSN: 1526-954X

L24 ANSWER 20 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Nontransgenic crops from transgenic plants
SO Nature Biotechnology (2002), 20(3), 215-216
CODEN: NABIF9; ISSN: 1087-0156

=> D TI SO 21-40

L24 ANSWER 21 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Switching on lineage tracers using site-specific recombination
SO Methods in Molecular Biology (Totowa, NJ, United States) (2002), 185(Embryonic Stem Cells), 309-334
CODEN: MMBIED; ISSN: 1064-3745

L24 ANSWER 22 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI ES cell-mediated conditional transgenesis
SO Methods in Molecular Biology (Totowa, NJ, United States) (2002), 185(Embryonic Stem Cells), 285-307
CODEN: MMBIED; ISSN: 1064-3745

L24 ANSWER 23 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Coping with kinetic and thermodynamic barriers: RMCE, an efficient strategy for the targeted integration of transgenes
SO Current Opinion in Biotechnology (2001), 12(5), 473-480
CODEN: CUOBE3; ISSN: 0958-1669

L24 ANSWER 24 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI A structural view of Cre-loxP site-specific recombination
SO Annual Review of Biophysics and Biomolecular Structure (2001), 30, 87-104
CODEN: ABBSE4; ISSN: 1056-8700

L24 ANSWER 25 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Control of directionality in integrase-mediated recombination: examination of recombination directionality factors (RDFs) including Xis and Cox proteins
SO Nucleic Acids Research (2001), 29(11), 2205-2216
CODEN: NARHAD; ISSN: 0305-1048

L24 ANSWER 26 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI The transgeneticist's toolbox: novel methods for the targeted modification of eukaryotic genomes
SO Biological Chemistry (2000), 381(9/10), 801-813
CODEN: BICHF3; ISSN: 1431-6730

L24 ANSWER 27 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Site-specific gene targeting for gene expression in eukaryotes
SO Current Opinion in Biotechnology (2000), 11(5), 455-460
CODEN: CUOBE3; ISSN: 0958-1669

L24 ANSWER 28 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Creating a transloxbation: engineering interchromosomal translocations in the mouse

SO EMBO Reports (2000), 1(2), 120-121
CODEN: ERMEAX; ISSN: 1469-221X

L24 ANSWER 29 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI New approaches towards ex vivo and in vivo gene therapy
SO Cells Tissues Organs (2000), 167(2-3), 75-80
CODEN: CTORFB; ISSN: 1422-6405

L24 ANSWER 30 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Geometry of the DNA substrates in Cre-loxP site-specific recombination
SO Proceedings of the Conversation in Biomolecular Stereodynamics, 11th, Albany, NY, United States, June 15-19, 1999 (2000), Volume Convers. 11, Issue 1, 141-146. Editor(s): Sarma, Ramaswamy H.; Sarma, Mukti H.
Publisher: Adenine Press, Schenectady, N. Y.
CODEN: 69AJOA

L24 ANSWER 31 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI The role of integrons in the dissemination of antibiotic resistance
SO Annales de Biologie Clinique (2000), 58(4), 439-444
CODEN: ABCLAI; ISSN: 0003-3898

L24 ANSWER 32 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Strategies and applications of the Cre/LoxP system in transgenic mice
SO Shengwu Huaxue Yu Shengwu Wuli Jinzhan (2000), 27(3), 235-238
CODEN: SHYCD4; ISSN: 1000-3282

L24 ANSWER 33 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Detection and analysis of gene expression during infection by in vivo expression technology
SO Philosophical Transactions of the Royal Society of London, Series B: Biological Sciences (2000), 355(1397), 587-599
CODEN: PTRBAE; ISSN: 0962-8436

L24 ANSWER 34 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Plasmid maintenance systems
SO Horizontal Gene Pool (2000), 49-85. Editor(s): Thomas, Christopher M.
Publisher: Harwood Academic Publishers, Amsterdam, Neth.
CODEN: 69ACPO

L24 ANSWER 35 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Structural homology between MarA of the AraC family of transcriptional activators and the integrase family of **site-specific recombinases**
SO Molecular Microbiology (2000), 35(6), 1582-1583
CODEN: MOMIEE; ISSN: 0950-382X

L24 ANSWER 36 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Brain region-specific and temporally restricted gene knockout using the Cre recombinase system
SO Techniques in the Behavioral and Neural Sciences (1999), 13(Handbook of Molecular-Genetic Techniques for Brain and Behavior Research), 282-290
CODEN: TBSCEC; ISSN: 0921-0709

L24 ANSWER 37 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Adenovirus vector
SO No no Kagaku (1999), 21(11), 1195-1200
CODEN: NNOKFZ; ISSN: 1343-4144

L24 ANSWER 38 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Analysis of mammalian cis-regulatory DNA elements by homologous recombination
SO Methods in Enzymology (1999), 306(Expression of Recombinant Genes in Eukaryotic Systems), 42-66
CODEN: MENZAU; ISSN: 0076-6879

L24 ANSWER 39 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI The integrase family of recombinases: organization and function of the active site
SO Molecular Microbiology (1999), 33(3), 449-456
CODEN: MOMIEE; ISSN: 0950-382X

L24 ANSWER 40 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Coming or going it's another pretty picture for the .lambda.-Int family album
SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(13), 7122-7124
CODEN: PNASA6; ISSN: 0027-8424

=> D TI SO 41-60

L24 ANSWER 41 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Reversible cell immortalization with the Cre-lox system
SO Human Gene Therapy (1999), 10(10), 1597-1598
CODEN: HGTHE3; ISSN: 1043-0342

L24 ANSWER 42 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Formation of extrachromosomal DNA rings in *Saccharomyces cerevisiae* using site-specific recombination
SO Methods in Molecular Biology (Totowa, New Jersey) (1999), 94(DNA Topoisomerase Protocols, Vol. 1), 125-133
CODEN: MMBIED; ISSN: 1064-3745

L24 ANSWER 43 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Mobile gene cassettes and integrons: moving antibiotic resistance genes in Gram-negative bacteria
SO Ciba Foundation Symposium (1997), 207(Antibiotic Resistance: Evolution, Selection and Spread), 192-205
CODEN: CIBSB4; ISSN: 0300-5208

L24 ANSWER 44 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Structure and mechanism in site-specific recombination
SO Current Opinion in Structural Biology (1999), 9(1), 14-20
CODEN: COSBEF; ISSN: 0959-440X

L24 ANSWER 45 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Antibiotic resistance in gram-negative bacteria: the role of gene cassettes and integrons
SO Drug Resistance Updates (1998), 1(2), 109-119
CODEN: DRUPFW; ISSN: 1368-7646

L24 ANSWER 46 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI A new method for gene knockout in mammalian cells
SO Jikken Igaku (1999), 17(2), 155-158
CODEN: JIIGEF; ISSN: 0288-5514

L24 ANSWER 47 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Recombinase-mediated gene integration in plants
SO Current Plant Science and Biotechnology in Agriculture (1998), 32(Somaclonal Variation and Induced Mutations in Crop Improvement), 501-516

CODEN: CPBAE2; ISSN: 0924-1949

L24 ANSWER 48 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Vaccinia virus DNA topoisomerase: a model eukaryotic type IB enzyme
SO Biochimica et Biophysica Acta (1998), 1400(1-3), 321-337
CODEN: BBACAQ; ISSN: 0006-3002

L24 ANSWER 49 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Teaching a new dog old tricks?
SO Structure (London) (1998), 6(5), 543-548
CODEN: STRUE6; ISSN: 0969-2126

L24 ANSWER 50 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Recombinase systems in plants
SO Biological Sciences Symposium, San Francisco, Oct. 19-23, 1997 (1997), 295-297 Publisher: TAPPI Press, Atlanta, Ga.
CODEN: 66GVA7

L24 ANSWER 51 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Inducible gene targeting in mice using the Cre/lox system
SO Methods (Orlando, Florida) (1998), 14(4), 381-392
CODEN: MTHDE9; ISSN: 1046-2023

L24 ANSWER 52 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Site-specific recombination caught in the act
SO Chemistry & Biology (1997), 4(10), 717-720
CODEN: CBOLE2; ISSN: 1074-5521

L24 ANSWER 53 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Site-specific recombination: synapsis and strand exchange revealed
SO Current Biology (1997), 7(10), R608-R612
CODEN: CUBLE2; ISSN: 0960-9822

L24 ANSWER 54 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Preparation of temporal or spacial gene targeting mouse in Cre/loxP system
SO Jikken Igaku (1997), 15(17), 2107-2113
CODEN: JIIGEF; ISSN: 0288-5514

L24 ANSWER 55 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Mechanisms of chromosomal translocations in malignant lymphomas
SO Molecular Biology of Hematopoiesis 5, [Proceedings of the Symposium on the Molecular Biology of Hematopoiesis], 9th, Genoa, June 23-27, 1995 (1996), Meeting Date 1995, 127-134. Editor(s): Abraham, Nader G. Publisher: Plenum, New York, N. Y.
CODEN: 64GMAY

L24 ANSWER 56 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Polynucleotidyl transfer reactions in site-specific DNA recombination
SO Genes to Cells (1997), 2(1), 1-12
CODEN: GECEFL; ISSN: 1356-9597

L24 ANSWER 57 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Conditional mutagenesis in mice: the Cre/loxP recombination system
SO International Journal of Experimental Pathology (1996), 77(6), 269-278
CODEN: IJEPEI; ISSN: 0959-9673

L24 ANSWER 58 OF 78 CAPLUS COPYRIGHT 2002 ACS
TI Construction of recombinant cell lines with defined properties using FLP recombinase driven gene replacement
SO Animal Cell Technology: From Vaccines to Genetic Medicine, [Proceedings of the Meeting of the EACT], 14th, Vilamoura, Port., May 1996 (1997),

Meeting Date 1996, 511-517. Editor(s): Carrondo, Manuel J. T.; Griffiths, Bryan; Moreira, Jose L. P. Publisher: Kluwer, Dordrecht, Neth. CODEN: 64ELAL

L24 ANSWER 59 OF 78 CAPLUS COPYRIGHT 2002 ACS

TI Targeted gene disruption: applications in neurobiology
SO Journal of Neuroscience Methods (1997), 71(1), 19-27
CODEN: JNMEDT; ISSN: 0165-0270

L24 ANSWER 60 OF 78 CAPLUS COPYRIGHT 2002 ACS

TI Recent advances in gene mutagenesis by site-directed recombination
SO Journal of Clinical Investigation (1996), 97(9), 1999-2002
CODEN: JCINAO; ISSN: 0021-9738

=> D IBIB AB 9,18,23,24,26,27,35,56,57

L24 ANSWER 9 OF 78 MEDLINE

ACCESSION NUMBER: 94167803 MEDLINE

DOCUMENT NUMBER: 94167803 PubMed ID: 8122308

TITLE: **Site-specific recombinases:**
tools for genome engineering.

AUTHOR: Kilby N J; Snaith M R; Murray J A

CORPORATE SOURCE: Institute of Biotechnology, University of Cambridge, UK.

SOURCE: TRENDS IN GENETICS, (1993 Dec) 9 (12) 413-21.
Ref: 51

Journal code: 8507085. ISSN: 0168-9525.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199404

ENTRY DATE: Entered STN: 19940412

Last Updated on STN: 19940412

Entered Medline: 19940405

AB **Site-specific recombinases** from bacteriophage and yeasts have been developed as novel tools for manipulating DNA both in the test-tube and in living organisms. We discuss the characteristics of these enzyme systems, review their application in genetic and developmental studies and speculate on their future potential for large-scale directed modifications of eukaryotic genomes.

L24 ANSWER 18 OF 78 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:325798 CAPLUS

DOCUMENT NUMBER: 137:150696

TITLE: Genome engineering using **site-specific recombinases**

AUTHOR(S): Kolb, Andreas F.

CORPORATE SOURCE: Cell Physiology Group, Hannah Research Institute, Ayr, UK

SOURCE: Cloning and Stem Cells (2002), 4(1), 65-80
CODEN: CSCLBO; ISSN: 1536-2302

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. The targeted modification of the mammalian genome has

a variety of applications in research, medicine, and biotechnol.

Site-specific recombinases have become significant tools in all of these areas. Conditional gene targeting using

site-specific recombinases has enabled the functional anal. of genes, which cannot be inactivated in the germline.

The **site-specific** integration of adeno-assocd. virus, a major gene therapy vehicle, relies on the **recombinase** activity

of the viral rep proteins. **Site-specific**

recombinases also allow the precise integration of open reading frames encoding pharmaceutically relevant proteins into highly active gene

loci in cell lines and transgenic animals. These goals have been accomplished by using a variety of genetic strategies but only a few recombinase proteins. However, the vast repertoire of recombinases, which

has recently become available as a result of large-scale sequencing projects, may provide a rich source for the development of novel strategies to precisely alter mammalian genomes.

REFERENCE COUNT: 84 THERE ARE 84 CITED

REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 23 OF 78 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:759526 CAPLUS

DOCUMENT NUMBER: 136:304568

TITLE: Coping with kinetic and thermodynamic barriers: RMCE,

an efficient strategy for the targeted integration of transgenes

AUTHOR(S): Baer, Alexandra; Bode, Jurgen

CORPORATE SOURCE: RDIF/Epigenetic Regulation, German Research Institute

for Biotechnology, Gesellschaft fur Biotechnologische Forschung mbH (GBF), Braunschweig, D-38124,

Germany

SOURCE: Current Opinion in Biotechnology (2001), 12(5), 473-480

CODEN: CUOBE3; ISSN: 0958-1669

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. **Site-specific**

recombinases have become powerful tools for the targeted integration of transgenes into defined chromosomal loci. They have been

successfully used both to achieve predictable gene expression in cell culture and for the systematic creation of transgenic animals. A recent

improvement of this method, the recombinase-mediated cassette exchange

procedure (RMCE), permits expression in the absence of any co-expressed

selection marker gene.

REFERENCE COUNT: 43 THERE ARE 43 CITED

REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 24 OF 78 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:482932 CAPLUS

DOCUMENT NUMBER: 135:191991

TITLE: A structural view of Cre-loxP site-specific recombination

AUTHOR(S): Van Duyne, Gregory D.

CORPORATE SOURCE: Department of Biochemistry and Biophysics, Howard

Hughes Medical Institute, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104, USA

SOURCE: Annual Review of Biophysics and Biomolecular Structure (2001), 30, 87-104

CODEN: ABBSE4; ISSN: 1056-8700

PUBLISHER: Annual Reviews Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 69 refs. Structural models of **site-specific recombinases**

from the lambda integrase family of enzymes have in the last four years provided an important new perspective on the three-dimensional nature of the recombination pathway.

Members of this family, which include the bacteriophage P1 Cre recombinase, bacteriophage lambda integrase, the yeast FLP recombinase, and the bacterial XerCD recombinases, exchange strands between DNA substrates in a stepwise process. One pair of strands is exchanged to form a Holliday junction intermediate, and the second pair of strands is exchanged during resolution of the junction to products. Crystal structures of reaction intermediates in the Cre-loxP site-specific recombination system, together with recent biochemical studies in the field, support a strand swapping model for recombination that does not require a branch migration of the Holliday junction intermediate in order to test homologous recombination sites.

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 26 OF 78 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:790924 CAPLUS
DOCUMENT NUMBER: 135:832
TITLE: The transgeneticist's toolbox: novel methods for the targeted modification of eukaryotic genomes
AUTHOR(S): Bode, Jürgen; Schlaake, Thomas; Iber, Michaela; Schubeler, Dirk; Seibler, Jost; Snejhkov, Evgeny; Nikolaev, Lev
CORPORATE SOURCE: German Center for Biotechnological Research (GBF), RDIF/Epigenetic Regulation, Braunschweig, D-38124, Germany
SOURCE: Biological Chemistry (2000), 381(9/10), 801-813
CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: Walter de Gruyter GmbH & Co. KG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 60 refs. Classical techniques for gene transfer into mammalian cells involve tedious screening procedures to identify transgenic clones or animals with the appropriate level and stability of expression or with the correct developmental patterns.

These first generation technologies are clearly inadequate for complex genetic strategies by which gene regulation can be studied in its entire complexity. While site-specific insertions can principally be achieved by homologous recombination or by adapting the recombination approach from phages or yeast, these methods usually lack the required efficiency or they perturb expression patterns by the co-insertion of prokaryotic vector parts. Virtually all of these problems can be overcome by recombinase-mediated cassette exchange (RMCE) techniques which cleanly

replace a resident cassette that is flanked by two hetero-specific recombination target sites for a second cassette with the analogous design, presented on a targeting vector. After illustrating the fundamentals of site-specific recombination by selected examples, the authors (arranged in the chronological order of their contribution) will describe their efforts to develop RMCE into a method of wide applicability. Further developments that have been initiated utilizing the particular potential of the RMCE principle will be outlined.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 27 OF 78 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:757589 CAPLUS
DOCUMENT NUMBER: 134:305816
TITLE: Site-specific gene targeting for gene expression in

eukaryotes

AUTHOR(S): Gorman, Cori; Bullock, Clayton
CORPORATE SOURCE: DNA Bridges, Inc., San Francisco, CA, 94117, USA
SOURCE: Current Opinion in Biotechnology (2000), 11(5), 455-460
CODEN: CUOBE3; ISSN: 0958-1669
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with refs. Major advances in the use of site-specific recombinases to facilitate sustained gene expression via chromosomal targeting have been made during the past year. New tools for genomic manipulations using this technology, including the discovery of epitopes in recombinases that confer nuclear localization, crystal structures that show the precise topology of recombinase-DNA-substrate synaptic complexes, manipulations of the DNA recognition sequences that select for integration over excision of DNA, and manipulations that make changes in gene expression inducible by drug administration. In addition, endogenous eukaryotic and mammalian DNA sequences have been discovered that can support site-specific recombinase-mediated manipulations.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 35 OF 78 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:261860 CAPLUS
DOCUMENT NUMBER: 133:27705
TITLE: Structural homology between MarA of the AraC family of transcriptional activators and the integrase family of site-specific recombinases
AUTHOR(S): Gillette, William K.; Rhee, Sanghee; Rosner, Judah L.; Martin, Robert G.
CORPORATE SOURCE: Laboratory of Molecular Biology, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Molecular Microbiology (2000), 35(6), 1582-1583
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with approx. 11 refs., on structural homology between MarA of the AraC family of transcriptional activators and the integrase family of site-specific recombinases.

L24 ANSWER 56 OF 78 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:246772 CAPLUS
DOCUMENT NUMBER: 126:312704
TITLE: Polynucleotidyl transfer reactions in site-specific DNA recombination
AUTHOR(S): Mizuuchi, Kiyoshi
CORPORATE SOURCE: Laboratory of Molecular Biology, National Institute of Diabetes, and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Genes to Cells (1997), 2(1), 1-12
CODEN: GECEFL; ISSN: 1356-9597
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with many refs. Site-specific DNA rearrangement reactions are widespread among organisms. They are used, for example, by vertebrates to boost immune response diversity, and in turn by

parasitic
 organisms to evade the host immune system by surface antigen switching.
 Parasitic genetic elements ubiquitous to most organisms invade new host
 genomic sites by a variety of types of site-specific recombination.
 Polynucleotidyl transfer reactions are central to these DNA recombination reactions. The recombinase of each reaction system that "catalyzes" such chem. reactions at specific DNA sites are apparently designed to accomplish unique DNA geometrical specificity, or delicate control over the extent or direction of the reaction, with the sacrifice of protein turnover. Here we discuss our current understanding of several issues that relate to the polynucleotidyl transfer steps in several of the better studied site-specific recombination reactions.

L24 ANSWER 57 OF 78 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:228322 CAPLUS
 DOCUMENT NUMBER: 126:234053
 TITLE: Conditional mutagenesis in mice: the Cre/loxP recombination system
 AUTHOR(S): Plueck, A.
 CORPORATE SOURCE: European Molecular Biology Laboratory, Cell Regulation
 Programme, Heidelberg, D-69012, Germany
 SOURCE: International Journal of Experimental Pathology
 (1996), 77(6), 269-278
 CODEN: IJEPET; ISSN: 0959-9673
 PUBLISHER: Blackwell
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English
 AB A review, with 15 refs., on the Cre/loxP site-specific recombinase system, its applications to gene targeting, cell type-specific gene targeting, gene targeting 'flox and delete' strategy, Cre transgenic mice, inducible gene targeting, and inducible and cell type-specific gene targeting.

=> dhis
 DHIS IS NOT A RECOGNIZED COMMAND
 The previous command name entered was not recognized by the system.
 For a list of commands available to you in the current file, enter
 "HELP COMMANDS" at an arrow prompt (=>).

=> d his

(FILE 'HOME' ENTERED AT 15:11:54 ON 15 OCT 2002)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 15:12:07 ON 15 OCT 2002
 L1 3018 S (CRE OR LOX OR FLP OR FRT) AND RECOMBINASE
 L2 2647 S (SELF OR AUTO)(S)(INACTIVAT? OR EXCISI?)
 L3 24 S L1 AND L2
 L4 15 DUP REM L3 (9 DUPLICATES REMOVED)
 L5 12 S SELFEXCIS? OR AUTOEXCIS?
 L6 0 S LI AND L5
 L7 1409345 S TOXIC?
 L8 81 S L1(S)L7
 L9 50 DUP REM L8 (31 DUPLICATES REMOVED)
 L10 405716 S TRANSIENT
 L11 31417 S TRANSIENT?(2A)EXPRESS?
 L12 6962 S RECOMBINASE
 L13 77 S L11(S)L12
 L14 33 DUP REM L13 (44 DUPLICATES REMOVED)
 L15 29 S L14 NOT PY>2000
 L16 2027 S (SITE DIRECTED OR SITE SPECIFIC)(S)RECOMBINASE
 L17 90 S L16 AND REVIEW
 L18 78 DUP REM L17 (12 DUPLICATES REMOVED)
 L19 425920 S IDENTIFY

L20 2125429 S IDENTIF?
 L21 8 S L18 AND L20
 L22 78 S L18
 L23 0 S T1 SO 1-20
 L24 78 S L18

=> log y
 COST IN U.S. DOLLARS SINCE FILE TOTAL
 ENTRY SESSION
 FULL ESTIMATED COST 231.44 231.65

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
 SINCE FILE TOTAL
 CA SUBSCRIBER PRICE -9.91 -9.91

STN INTERNATIONAL LOGOFF AT 16:43:24 ON 15 OCT 2002